

The conserved cysteine residue of type III intermediate filaments serves as a structural element and redox sensor.

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Glial fibrillary acidic protein (GFAP) along with vimentin, desmin and peripherin constitutes the type III class of intermediate filament proteins, which are expressed in a cell type-dependent manner. GFAP and vimentin play a role in organelle positioning, cell migration and mechanical resistance and possess a conserved cysteine residue (cys328 in vimentin and cys294 in GFAP). We previously showed that cys328 of vimentin is critical for stress sensing, since mutants lacking this residue are resistant to vimentin reorganization induced by oxidants and electrophilic lipids. We have recently observed that cys294 of GFAP is also a target for lipoxidation, which induces a drastic filament rearrangement in cells. Importantly, the cys294ser mutant is resistant to these effects, thus implying its critical role in the cellular response to oxidative damage. However, this mutant displays defective assembly and copolymerization with vimentin, showing that the single cysteine residue is important for the structure of the intermediate filament network. This strengthens the hypothesis that modifications of cysteine residues of intermediate filaments may contribute to cellular dysfunction under pathophysiological conditions.

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